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Review

Green Synthesis of Functional Nanostructures: A Mini-Review of Strategies, Applications, and Challenges

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Abstract

The development of biocompatible functional nanostructures has emerged as a key driver in advancing nanomedicine, environmental remediation, and sustainable energy technologies. However, conventional synthesis methods often rely on toxic reagents, hazardous solvents, and energy-intensive processes, raising significant concerns regarding environmental impact and biological safety. In this context, green synthesis has gained increasing attention as a sustainable alternative, utilizing biological systems, renewable resources, and environmentally benign solvents to produce functional nanomaterials. This mini-review provides an overview of recent advances in the green synthesis of organic, inorganic, and hybrid nanostructures, highlighting their physicochemical properties and functional performance. Particular emphasis is placed on their applications in nanomedicine, including drug delivery, bioimaging, antimicrobial and anticancer therapies, and theranostic platforms. Additionally, their roles in environmental applications, such as pollutant degradation and water treatment, and in energy-related systems, including catalysis, solar energy conversion, and energy storage, are discussed with selected representative examples. Despite significant progress, key challenges remain, including limited mechanistic understanding, reproducibility issues, scalability constraints, and uncertainties related to long-term toxicity and environmental impact. Addressing these limitations will be essential for the safe and large-scale implementation of green nanotechnology. Overall, the integration of green chemistry principles with advanced nanomaterial design offers a promising pathway toward the development of multifunctional, sustainable, and high-performance nanostructures capable of addressing global health, environmental, and energy challenges.

Keywords: green synthesis; biocompatible nanostructures; nanomedicine; drug delivery; bioimaging; environmental remediation; energy applications; theranostics

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1. Introduction

The rapid evolution of nanotechnology has enabled the design and fabrication of functional nanostructures with unprecedented control over size, morphology, and surface chemistry. These features confer unique physicochemical properties, including high surface-to-volume ratios, quantum confinement effects, and tunable reactivity, positioning nanomaterials at the forefront of innovation in nanomedicine, environmental remediation, and energy technologies [1–3]. In particular, nanomedicine has emerged as a transformative field, offering advanced solutions for targeted drug delivery, bioimaging,

biosensing, and theranostic applications [4–6]. These approaches have significantly improved diagnostic accuracy and therapeutic efficiency, contributing to the development of personalized medicine.

Despite these advances, conventional methods for synthesizing nanostructures often rely on toxic chemicals, hazardous reducing agents, and energy-intensive processes, raising serious concerns regarding environmental sustainability and biological safety [1,7]. The presence of residual toxic reagents can compromise the applicability of nanomaterials in biomedical contexts, where strict safety requirements must be met.

In this context, green synthesis has emerged as a promising alternative, utilizing biological systems such as plant extracts, agro-industrial residues, and microorganisms to produce nanomaterials under environmentally benign conditions [8,9]. These approaches not only reduce environmental impact but also enhance the biocompatibility and functional properties of the resulting nanostructures.

Although green synthesis is widely associated with enhanced biocompatibility, this assumption should be interpreted with caution. The use of biological systems and naturally derived compounds can reduce the reliance on toxic reagents and introduce functional surface groups; however, the resulting biocompatibility is not intrinsic and depends on multiple factors, including nanoparticle size, morphology, surface chemistry, concentration, and exposure conditions [10]. Moreover, variations in biological sources may lead to inconsistencies in physicochemical properties, directly affecting biological interactions and safety profiles [11]. Therefore, a critical evaluation of green-synthesized nanostructures is necessary, not only to highlight their potential advantages but also to address current limitations, reproducibility challenges, and the need for standardized toxicological assessment [12].

In this context, this mini-review aims to provide a critical overview of green synthesis strategies and their applications in nanomedicine, environmental remediation, and energy systems, with particular emphasis on existing challenges and future research directions. This work is intentionally structured as a concise mini-review, focusing on representative examples and key performance metrics rather than exhaustive coverage of the field.

Beyond nanomedicine, green-synthesized nanomaterials have shown promising performance in environmental and energy applications. In environmental systems, they are widely used for pollutant degradation, water purification, and antimicrobial treatments [13,14]. In the energy sector, nanostructured materials contribute to improved catalytic performance, solar energy conversion, and advanced energy storage systems [15,16].

Although substantial progress has been achieved, several challenges remain, including limited mechanistic understanding, reproducibility issues, and scalability constraints [7,12]. Addressing these challenges will be essential for translating green nanotechnology into practical and industrial applications.

In this mini-review, we provide a critical analysis of recent developments in green-synthesized functional nanostructures, emphasizing not only their applications in nanomedicine, environmental remediation, and energy systems, but also the current limitations, comparative challenges, and key knowledge gaps that must be addressed to enable their practical and scalable implementation. It is important to note that this mini-review primarily focuses on metal-based and hybrid nanostructures synthesized via green approaches, as these systems represent the most extensively studied and technologically relevant class of materials in this field. Other types of nanostructures are mentioned when relevant, but are not the central focus of this work.

Rather than focusing on a single application domain, this mini-review adopts an interdisciplinary perspective to highlight common mechanisms, comparative performance, and shared challenges of green-synthesized metal-based and hybrid nanomaterials across nanomedicine, environmental, and energy applications. This approach enables the identifi-

cation of cross-cutting limitations and opportunities that may not be evident in domain-specific analyses.

2. Green Synthesis of Functional Nanostructures

The increasing concern over environmental sustainability and biological safety has driven the transition from conventional physicochemical synthesis methods toward greener and more sustainable approaches for the production of functional nanostructures. Traditional synthesis routes often involve toxic reagents, hazardous solvents, and high-energy consumption, which not only generate environmentally harmful byproducts but also compromise the biocompatibility of the resulting nanomaterials [1,2,7].

In contrast, green synthesis offers an eco-friendly alternative by employing renewable resources, benign reaction conditions, and energy-efficient processes, while maintaining control over nanoparticle size, morphology, and functionality [17,18]. Recent advances have also explored the integration of artificial intelligence and machine learning to improve control over nanoparticle synthesis, predictively model nano-bio interactions, and optimize nanopharmaceutical formulations [19].

Green synthesis strategies are generally based on three main principles: the use of biological systems as reducing and stabilizing agents, the replacement of toxic solvents with environmentally benign alternatives (such as the valorization of agro-industrial residues and plant hydrolates), and the adoption of low-energy or hybrid synthesis techniques [1,7]. These approaches not only reduce environmental waste but also introduce intrinsic functionalization, which is particularly advantageous for biomedical applications [2,8,20]. A schematic overview of the green synthesis process and the resulting functional nanostructures is presented in Figure 1.

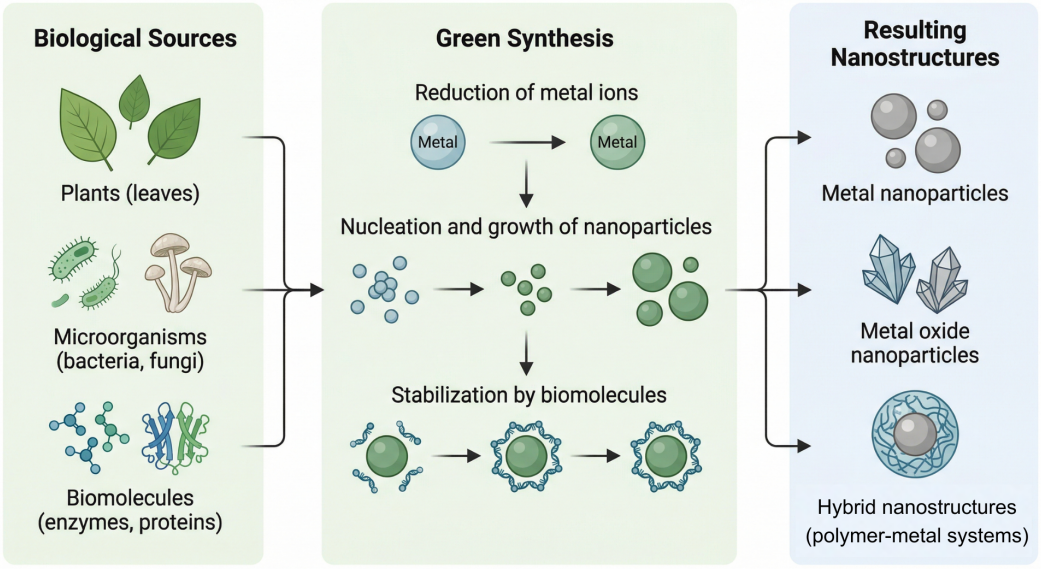


Figure 1. Schematic illustration of green synthesis of functional nanostructures based on biological and polymer–metal systems. Biological sources, including plants, microorganisms, biomolecules, and polymeric matrices, act as reducing and stabilizing agents, enabling the formation of nanostructures under environmentally benign conditions. The process involves reduction of metal ions, followed by nucleation, growth, and stabilization through biomolecular or polymeric capping, resulting in nanostructures with tunable physicochemical properties for diverse applications. Source: Created by the authors.

2.1. Biological Routes

Biological synthesis has emerged as a cornerstone of green nanotechnology, utilizing naturally derived biomolecules and living organisms to mediate nanoparticle formation [18,20]. Among these, plant-mediated synthesis is one of the most widely explored methods due to its simplicity, scalability, and cost-effectiveness [2,17]. Plant extracts and derivatives—including essential oils and hydrolates—contain a diverse array of phytochemicals, such as flavonoids, polyphenols, terpenoids, and alkaloids, which act simultaneously as reducing and capping agents [6,21]. This dual role enables the formation of stable nanostructures without the need for additional chemical stabilizers, thereby enhancing biocompatibility [8].

Microbial synthesis, involving bacteria, fungi, and algae, provides an alternative approach with greater control over nanoparticle size and morphology [8,12]. These organisms can facilitate both intracellular and extracellular synthesis through enzymatic reactions and metabolic pathways [8]. Despite their advantages in producing well-defined nanostructures, microbial methods often require controlled growth conditions, longer synthesis times, and more complex downstream processing, which may limit their large-scale applicability [12].

Enzyme-assisted synthesis represents a more controlled biological route, where specific enzymes catalyze nanoparticle formation under mild conditions [1,22]. This approach offers high selectivity and reproducibility, allowing precise tuning of nanoparticle properties. However, the high cost of enzymes and challenges related to their stability may restrict widespread implementation [7].

At the mechanistic level, biological synthesis of nanostructures is primarily governed by redox reactions mediated by biomolecules such as polyphenols, proteins, enzymes, and reducing sugars. These compounds facilitate the reduction of metal ions into their corresponding nanoparticles while simultaneously acting as capping agents, stabilizing the formed structures and preventing aggregation [21]. In addition to the biochemical composition of biological systems, physicochemical parameters such as pH, temperature, and precursor concentration play a crucial role in determining nanoparticle formation and properties. Variations in pH can alter the ionization state of biomolecules, influencing their reducing capacity and binding affinity to nanoparticle surfaces, which directly affects nucleation and stabilization processes [20]. Temperature governs reaction kinetics, where higher temperatures generally accelerate reduction rates and nucleation, often leading to smaller particle sizes, while lower temperatures may favor slower growth and broader size distributions [23]. Precursor concentration influences supersaturation levels, impacting nucleation density and particle aggregation [1]. These mechanistic and physicochemical aspects are essential for achieving reproducible and tunable green synthesis of nanostructures.

2.2. Green Solvents and Low-Energy Techniques

The selection of solvents plays a critical role in determining the sustainability and safety of nanomaterial synthesis [1]. Water is the most commonly used green solvent due to its non-toxic nature, abundance, and compatibility with biological systems. Nevertheless, emerging solvent systems such as ionic liquids and deep eutectic solvents has gained increasing interest owing to their unique physicochemical properties, including low volatility, high thermal stability, and tunable polarity [2,22].

These solvents can enhance nanoparticle stability, control nucleation processes, and enable the synthesis of complex nanostructures under relatively mild conditions [20]. However, their large-scale application requires careful evaluation of toxicity, cost, and recyclability [7].

From a mechanistic perspective, green solvents such as water, ionic liquids, and deep eutectic solvents influence nanoparticle formation by modifying solvation dynamics, ion mobility, and nucleation pathways [1]. For instance, ionic liquids can stabilize intermediate species and control crystal growth through strong electrostatic interactions, while deep eutectic solvents provide tunable hydrogen-bonding networks that affect precursor reduction and particle stabilization [22]. In low-energy techniques, microwave-assisted synthesis promotes rapid and uniform heating, leading to homogeneous nucleation and reduced particle size distribution [3], whereas ultrasound-assisted methods generate localized high-energy conditions through acoustic cavitation, enhancing mass transfer and nucleation rates [24]. These approaches contribute to improved control over nanoparticle properties while reducing energy consumption and environmental impact [23].

In parallel, low-energy synthesis techniques have been developed to reduce energy consumption and improve process efficiency. Microwave-assisted synthesis enables rapid and uniform heating, significantly shortening reaction times and improving nanoparticle homogeneity [3]. Ultrasound-assisted methods rely on acoustic cavitation to promote nucleation and dispersion, leading to better control over particle size and morphology [24]. Additionally, photochemical and light-driven processes offer sustainable alternatives by utilizing renewable energy sources, further reducing the environmental footprint of nanomaterial production [23].

2.3. Hybrid and Multifunctional Nanostructures

The development of hybrid and multifunctional nanostructures represents a key advancement in green nanotechnology [20]. By integrating organic and inorganic components, these systems can combine multiple functionalities—such as optical, magnetic, catalytic, and biological properties—within a single platform [6].

Green synthesis approaches have been successfully applied to the fabrication of such hybrid systems, often using supramolecular polymer networks, nanogels, emulgels, or polysaccharides as templates and stabilizing matrices [6,25]. These materials not only improve nanoparticle stability but also introduce additional functional groups that facilitate further modification and application [3].

Multifunctional nanostructures are particularly relevant for complex applications that require synergistic effects. In nanomedicine, they enable the development of theranostic platforms that combine imaging and therapy [4]. In environmental applications, they can simultaneously perform adsorption and catalytic degradation of pollutants [13]. In energy systems, hybrid nanostructures contribute to improved catalytic efficiency and charge transfer [16].

Despite these advances, challenges remain in achieving precise control over the structure–function relationship in hybrid systems, as well as ensuring reproducibility and scalability [7,12]. Addressing these limitations will be essential for translating green-synthesized multifunctional nanostructures into practical applications.

From a structural and functional perspective, hybrid nanostructures are formed through the integration of distinct material components, where interfacial interactions play a critical role in determining overall performance [6]. These interactions may include electrostatic forces, covalent bonding, hydrogen bonding, and van der Waals interactions, which influence charge transfer, catalytic activity, and structural stability [25]. In green synthesis approaches, biomolecules and biopolymers often act as templates or bridging agents, facilitating controlled assembly and functional integration [3]. The resulting hybrid systems can exhibit synergistic effects, where the combined properties of individual components lead to enhanced optical, catalytic, or biological performance [20]. However, achieving precise control over composition, interface structure, and functional balance re-

mains a significant challenge for reproducible and scalable synthesis [7]. Table 1 provides a comparative overview of representative green-synthesized metal-based and hybrid nanomaterials, highlighting their synthesis routes, physicochemical characteristics, and application performance.

Table 1. Representative green-synthesized metal-based and hybrid nanomaterials, their synthesis conditions and application performance.

Nanomaterial	Synthesis Route	Size (nm)	Morphology	Application
Ag nanoparticles	Plant-mediated	10–50	Spherical	Antimicrobial Performance: High antibacterial activity and inhibition efficiency
Au nanoparticles	Microbial	5–30	Spherical	Drug delivery Performance: Enhanced cellular uptake and improved targeting efficiency
ZnO nanoparticles	Green solvent-assisted	20–80	Rods, spherical	Photocatalysis Performance: High degradation rate of organic pollutants
Fe_3O_4 nanoparticles	Hybrid (biopolymer)	10–60	Core–shell	Water treatment Performance: Efficient heavy metal adsorption capacity
Carbon-based nanocomposites	Hybrid	20–100	Composite	Energy storage Performance: High capacitance and excellent cycling stability

3. Applications

Although green-synthesized nanostructures have been widely explored across nanomedicine, environmental, and energy applications, the depth of investigation varies significantly among these domains [2,22]. In many cases, reported studies focus on proof-of-concept demonstrations rather than systematic comparisons or long-term performance evaluation [3,7]. Therefore, a critical examination of these applications is necessary to distinguish well-established advances from emerging or still-limited approaches, as well as to identify the main challenges that hinder their practical implementation [1,12].

In addition to summarizing applications, this section emphasizes a critical and comparative perspective across different domains, highlighting variations in performance metrics, scalability, and practical limitations. Representative examples are discussed to provide a more quantitative and application-oriented analysis.

The application of green-synthesized metal-based and hybrid nanomaterials has expanded significantly across multiple scientific and technological domains [17,23]. Owing to their tunable physicochemical properties and surface functionalization, these nanomaterials have demonstrated remarkable versatility in nanomedicine, environmental remediation, and energy-related systems [8,9,26].

This versatility enables their use across a wide range of applications, as illustrated in Figure 2 [20]. Although Figure 2 provides a general overview of these application domains, the actual performance of green-synthesized metal-based and hybrid nanomaterials depends strongly on synthesis conditions, material composition, and application-specific parameters.

Green-synthesized nanostructures enable a wide range of multifunctional applications. In nanomedicine, they support advanced diagnostic and therapeutic platforms, including targeted drug delivery, bioimaging, biosensing, gene delivery, and theranostic cancer therapy [4–6]. In environmental systems, these nanomaterials contribute to water purification, antimicrobial treatment, pollutant degradation, air pollutant removal, and heavy metal removal through adsorption and catalytic processes [3,13]. In energy applications, they play a critical role in solar energy conversion, hydrogen production, and the development of high-performance energy storage systems [14–16].

The convergence of these applications highlights the interdisciplinary nature of sustainable nanotechnology and its potential to address global challenges in healthcare,

environmental protection, and clean energy [1,15,22]. In the following subsections, the specific mechanisms and roles of green-synthesized nanostructures in each domain are discussed in detail. Table 1 summarizes representative green-synthesized metal-based and hybrid nanomaterials, highlighting their synthesis routes, physicochemical characteristics, and application performance.

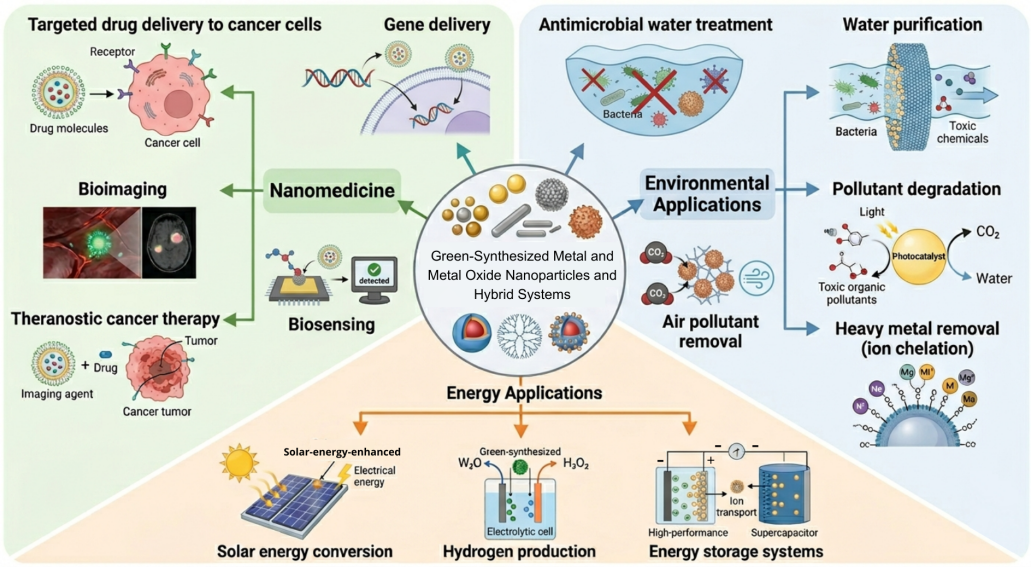


Figure 2. Representative applications of green-synthesized metal-based and hybrid nanomaterials across nanomedicine, environmental remediation, and energy systems. In nanomedicine, these materials enable targeted drug delivery, gene delivery, bioimaging, biosensing, and theranostic cancer therapy, primarily based on metal and metal oxide nanoparticles functionalized with biological or polymeric components. In environmental applications, they contribute to water purification, antimicrobial treatment, pollutant degradation, air pollutant removal, and heavy metal removal through adsorption and catalytic processes. In the energy sector, they are involved in solar energy conversion, hydrogen production via catalytic water splitting, and advanced energy storage systems. The figure highlights the multifunctional nature of these systems and their relevance in sustainable nanotechnology. Arrows indicate representative application pathways, while the red "X" denotes microbial inhibition/removal in antimicrobial water treatment. Colors and patterns are used only for schematic differentiation. Source: Created by the authors.

3.1. Nanomedicine Applications

Nanomedicine applications based on green-synthesized metal and hybrid nanomaterials have significantly advanced the development of innovative diagnostic and therapeutic strategies [3,8,20]. In particular, metal and metal oxide nanoparticles synthesized via green approaches offer advantages such as reduced toxicity, intrinsic surface functionalization, and improved interactions with biological systems [5,21]. These features make them suitable for applications including targeted drug delivery, bioimaging, and biosensing, where safety, efficiency, and controlled functionality are critical. As a result, green nanotechnology has become an important driver in the development of nanomaterial-based therapeutic and diagnostic systems [3,6].

3.2. Drug Delivery and Controlled Release

Nanostructured systems—including green-synthesized nanogels, polymeric micelles, and emulgels—have transformed conventional drug delivery approaches by enabling targeted transport and controlled release of therapeutic agents [3,8]. Biocompatible nanoparticles synthesized via green methods often possess surface functional groups derived from biological precursors, which facilitate drug loading and improve

cellular uptake [20,21]. Targeted delivery can be achieved through passive or active mechanisms. Passive targeting is primarily based on the enhanced permeability and retention (EPR) effect, which allows nanoparticles to accumulate in tumor tissues due to their leaky vasculature [4]. However, the heterogeneity of the EPR effect across different tumor types remains a limitation, necessitating the development of more precise targeting strategies [7]. Active targeting involves the functionalization of metal-based and hybrid nanomaterials with ligands such as antibodies, peptides, or small molecules that selectively bind to overexpressed receptors on diseased cells [18]. Green synthesis offers an advantage in this context by enabling surface functionalization during nanoparticle formation, reducing the need for post-synthetic chemical modifications [21]. Controlled release systems based on stimuli-responsive metal-based and hybrid nanomaterials have further improved therapeutic efficiency [3,19]. These systems respond to internal stimuli such as pH, redox conditions, and enzymatic activity, or external triggers such as temperature, light, and magnetic fields. Such responsiveness enables site-specific drug release, minimizing systemic toxicity and enhancing therapeutic outcomes [19]. Despite the significant advances in targeted drug delivery, most green-synthesized nanostructures are still evaluated under simplified experimental conditions, often lacking direct comparison with conventionally synthesized nanocarriers. In addition, variability in biological synthesis routes may lead to inconsistencies in particle size, surface functionality, and drug loading efficiency, which can compromise reproducibility and translational potential. These limitations highlight the need for standardized evaluation protocols and more systematic in vivo studies to validate their clinical applicability.

Representative studies provide quantitative insights into performance metrics and application-specific outcomes, including drug loading efficiency, IC_{50} values, imaging performance, and antimicrobial activity, highlighting how green-synthesized nanomaterials can be systematically evaluated in biomedical contexts. Recent studies have demonstrated the practical potential of green-synthesized nanomaterials in biomedical applications with measurable performance outcomes. For example, plant-mediated silver and gold nanoparticles have been reported for targeted drug delivery in cancer models, achieving drug loading efficiencies above 70% and enhanced cytotoxicity compared to free drugs, with IC_{50} values significantly reduced in breast and lung cancer cell lines [3,20]. Similarly, green-synthesized iron oxide nanoparticles have shown improved contrast enhancement in magnetic resonance imaging (MRI), with increased signal intensity and favorable biocompatibility profiles in in vitro and in vivo models [4,22]. In antimicrobial applications, biosynthesized metallic nanoparticles have demonstrated strong activity against multidrug-resistant strains, with low minimum inhibitory concentration (MIC) values and reduced toxicity toward mammalian cells [9,18]. Despite these promising results, the translation of these systems to clinical applications remains limited. Key challenges include variability in nanoparticle size distribution, lack of standardized synthesis protocols, and inconsistent biodistribution profiles. In particular, the reliance on the enhanced permeability and retention (EPR) effect has shown limited reproducibility in human tumors, raising concerns about targeting efficiency in clinical settings [4]. Therefore, future research should focus on improving targeting strategies, conducting systematic in vivo validation, and establishing standardized evaluation frameworks to better assess clinical translatability.

3.3. Bioimaging and Biosensing

Metal-based and hybrid nanomaterials have played a crucial role in improving the sensitivity and resolution of imaging and biosensing technologies [8,20]. Materials such as gold nanoparticles, quantum dots, and magnetic nanostructures exhibit unique optical

and magnetic properties that make them ideal for use as contrast agents and signal amplifiers [3,6]. Green synthesis contributes to the development of safer imaging agents by reducing cytotoxicity and improving colloidal stability in physiological environments [2]. In particular, biologically derived capping agents can enhance circulation time and reduce immune recognition, thereby improving in vivo imaging performance [21]. In biosensing applications, metal-based and hybrid nanomaterials enable rapid and highly sensitive detection of biomolecules, pathogens, and disease markers [6,20]. Their high surface area and tunable surface chemistry allow for selective interaction with target analytes, generating measurable optical, electrochemical, or magnetic signals. The integration of green-synthesized nanomaterials into biosensors supports the development of portable and point-of-care diagnostic devices [8]. Although green-synthesized nanostructures have improved the safety profile of imaging and biosensing systems, their performance is still often evaluated under controlled laboratory conditions, with limited validation in complex biological environments. In addition, issues related to signal stability, long-term circulation, and potential interference from biological matrices remain insufficiently explored. These challenges highlight the need for more robust in vivo studies and standardized evaluation protocols to fully assess their diagnostic reliability and clinical potential.

3.4. Antimicrobial and Anticancer Applications

Green-synthesized nanomaterials have demonstrated significant potential in antimicrobial and anticancer therapies [8,20]. Metallic nanoparticles, particularly silver, gold, and zinc oxide, exhibit strong antimicrobial activity against a wide range of pathogens [5,9]. The antimicrobial mechanisms are generally associated with the generation of reactive oxygen species (ROS), disruption of cell membranes, and interference with intracellular processes [5]. Importantly, the presence of bioactive compounds from biological synthesis routes, such as essential oils and plant hydrolates, can enhance these effects, leading to synergistic antimicrobial activity [2,21]. In cancer therapy, metal-based and hybrid nanomaterials enable targeted delivery of chemotherapeutic agents and can also act as therapeutic agents through mechanisms such as photothermal therapy, photodynamic therapy (PDT), and ROS-mediated apoptosis [3,5]. In PDT applications, for instance, nanostructured delivery platforms help stabilize natural photosensitizers, managing competing photophysical decay pathways—such as minimizing non-radiative internal conversion ($S_1 \rightarrow S_0$)—to favor efficient intersystem crossing and subsequent ROS generation [5]. However, challenges related to selectivity, biodistribution, and long-term toxicity remain critical barriers to clinical translation [7]. Despite the promising antimicrobial and anticancer properties of green-synthesized nanomaterials, most studies are limited to in vitro evaluations, with relatively few comprehensive in vivo or clinical investigations. Additionally, the mechanisms of action are often described in general terms, lacking detailed understanding of dose-dependent effects, long-term toxicity, and potential off-target interactions. These limitations underscore the need for more systematic biological validation and mechanistic studies to ensure safe and effective therapeutic applications.

3.5. Theranostic Platforms

Theranostics represents a rapidly evolving field that integrates diagnostic and therapeutic functionalities within a single nanostructured platform [3,20]. These systems enable real-time monitoring of disease progression and treatment response, supporting the development of personalized medicine [18]. Biocompatible hybrid nanostructures are particularly well-suited for theranostic applications, as they can incorporate imaging agents, drug delivery systems, and targeting ligands into a unified architecture [6]. Green synthesis approaches facilitate the integration of these components while min-

imizing toxicity and improving overall system stability [3,21]. Recent advances have demonstrated the potential of multifunctional metal-based and hybrid nanomaterials in applications such as image-guided therapy, combined chemo-photothermal treatments, and multimodal imaging [3,5]. Despite these promising developments, challenges related to regulatory approval, large-scale production, and clinical validation require further investigation [7].

Although theranostic platforms based on green-synthesized nanostructures offer significant potential for integrated diagnosis and therapy, their practical implementation remains limited by challenges in system complexity, reproducibility, and regulatory approval. The integration of multiple functionalities within a single nanostructure can lead to variability in performance and difficulties in large-scale manufacturing. Furthermore, the lack of standardized validation protocols hinders the comparison of different systems and slows down clinical translation.

3.6. Environmental Applications

Green-synthesized metal-based and hybrid nanomaterials have emerged as effective materials for addressing critical environmental challenges, particularly in water treatment, pollutant degradation, and remediation of contaminated ecosystems [3,20,26]. Their high surface area, tunable surface chemistry, and catalytic properties enable efficient interaction with a wide range of contaminants, including organic pollutants, heavy metals, and emerging contaminants such as pharmaceuticals and microplastics [8,9].

3.7. Pollutant Degradation and Photocatalysis

Representative studies in environmental applications provide quantitative evidence of the performance of green-synthesized nanomaterials under different operational conditions. For instance, green-synthesized ZnO and TiO_2 nanoparticles have demonstrated high degradation efficiencies (>90%) for organic dyes such as methylene blue and rhodamine B under UV or visible irradiation, with reaction times significantly reduced compared to conventional catalysts [9,26]. Similarly, iron oxide-based nanocomposites have shown adsorption capacities exceeding 100 mg g^{-1} for heavy metals such as Pb^{2+} and Cd^{2+}, highlighting their effectiveness in water treatment systems [13,25]. Despite these promising results, most studies are conducted under simplified laboratory conditions, often neglecting the complexity of real environmental systems. Factors such as competing ions, natural organic matter, and variable pH conditions can significantly affect performance. Therefore, future work should prioritize testing under realistic conditions and long-term stability assessments to ensure practical applicability.

Photocatalytic nanomaterials play a central role in the degradation of organic pollutants in water and air [9,20]. Metal oxide nanostructures, such as titanium dioxide (TiO_2) and zinc oxide (ZnO), are widely used due to their strong oxidative capabilities under light irradiation [3]. Green synthesis methods enhance the sustainability of these materials while often introducing surface functional groups that improve photocatalytic efficiency [9,26]. Under light exposure, these nanostructures generate reactive oxygen species (ROS), including hydroxyl radicals and superoxide ions, which can effectively degrade dyes, pesticides, and pharmaceutical residues into less harmful compounds [9]. The use of green-synthesized nanomaterials not only reduces the environmental impact of their production but also improves their stability and reusability, which are critical for large-scale applications [2]. Recent studies have also explored the incorporation of dopants and the development of hybrid nanostructures to extend light absorption into the visible region, thereby enhancing photocatalytic performance under solar irradiation [16].

These advancements are essential for the development of energy-efficient and sustainable remediation technologies [3].

Despite the demonstrated efficiency of green-synthesized photocatalytic nanomaterials, many studies are conducted under idealized laboratory conditions, which may not accurately represent real environmental systems. Factors such as complex pollutant mixtures, variable pH, and the presence of competing ions can significantly affect performance. In addition, issues related to catalyst recovery, long-term stability, and reusability remain insufficiently addressed, highlighting the need for more realistic and scalable evaluation approaches.

3.8. Heavy Metal Removal and Water Treatment

The removal of heavy metals from water systems is a major environmental concern due to their toxicity, persistence, and bioaccumulation [3,20]. Green-synthesized metal-based and hybrid nanomaterials have demonstrated excellent adsorption capacities for metal ions such as lead (Pb^{2+}), cadmium (Cd^{2+}), mercury (Hg^{2+}), and arsenic (As^{3+}) [2,26]. The effectiveness of these nanomaterials is largely attributed to their high surface area and the presence of functional groups, such as hydroxyl, carboxyl, and amine groups, which facilitate strong interactions with metal ions [3]. Biosynthesized nanoparticles and nanocomposites, particularly those incorporating biopolymers or carbon-based materials, exhibit enhanced adsorption performance and selectivity [8,20]. In addition to adsorption, some nanostructures can reduce or transform toxic metal ions into less harmful forms through catalytic processes [2]. The integration of adsorption and catalytic functionalities in a single material further enhances the efficiency of water treatment systems [9]. Although green-synthesized nanostructures exhibit high adsorption capacities for heavy metal removal, most studies are performed using simplified aqueous systems that do not reflect the complexity of real wastewater. The presence of competing ions, organic matter, and fluctuating environmental conditions can significantly influence adsorption efficiency and selectivity. Moreover, challenges related to material recovery, regeneration, and potential secondary contamination remain insufficiently addressed, limiting large-scale applicability.

3.9. Multifunctional Nanomaterials for Environmental Remediation

The development of multifunctional metal-based and hybrid nanomaterials represents a significant advancement in environmental applications [3,20]. These systems are capable of performing multiple tasks simultaneously, such as adsorption, catalytic degradation, and antimicrobial activity, making them highly effective for complex environmental systems [3]. Green synthesis plays a key role in enabling the fabrication of such multifunctional materials, often through the use of biological templates or hybridization strategies [26]. For example, nanocomposites combining metal oxides with carbon-based materials or biopolymers can exhibit synergistic effects, leading to improved performance compared to single-component systems [16,20]. Moreover, the biocompatibility and reduced toxicity of green-synthesized nanomaterials minimize secondary environmental risks, which is particularly important for applications involving direct interaction with natural ecosystems [2,21]. Despite the advantages of multifunctional nanomaterials, their performance is often evaluated under controlled conditions that do not capture the complexity of real environmental systems. The integration of multiple functionalities may also introduce challenges related to stability, reproducibility, and potential interference between different active components. Furthermore, the long-term environmental impact and ecological risks of these materials remain insufficiently understood, highlighting the need for comprehensive life cycle assessments and field-scale validation.These considerations are consistent

with existing challenges in the field, including the recovery and reuse of nanomaterials after treatment, potential ecotoxicological effects, and the scalability of green synthesis methods [7]. Addressing these issues will be essential for the practical implementation of nanotechnology-based environmental solutions.

3.10. Energy Applications

The growing global demand for clean and sustainable energy has accelerated the development of advanced nanomaterials with enhanced catalytic, electronic, and structural properties [15,17]. In this context, green-synthesized metal-based and hybrid nanomaterials have emerged as promising candidates for a wide range of energy-related applications, including catalysis, solar energy conversion, and energy storage systems [16,20]. Their tunable physicochemical characteristics enable improved performance in next-generation energy technologies [15,26].

3.11. Catalysis for Energy Conversion

Nanostructured materials play a crucial role in catalytic processes associated with energy conversion, such as hydrogen production, fuel cells, and carbon dioxide reduction [15]. Green-synthesized nanoparticles, particularly metal and metal oxide nanostructures, exhibit high catalytic activity due to their large surface area and abundant active sites [16,20]. In hydrogen production, nanocatalysts are widely used in water-splitting reactions, where they facilitate the hydrogen evolution reaction (HER) and oxygen evolution reaction (OER) [13]. Green synthesis methods can produce catalysts with controlled morphology and surface functionality, improving catalytic efficiency while minimizing environmental impact [26]. Similarly, in fuel cell technologies, nanomaterials are employed as electrocatalysts to enhance reaction kinetics and reduce energy losses [15,16]. The use of green-synthesized metal-based and hybrid nanomaterials contributes to the development of more efficient and potentially safer catalytic systems [8]. Despite the high catalytic activity reported for green-synthesized nanomaterials, most studies focus on short-term performance under controlled conditions, with limited evaluation of long-term stability and durability. In addition, direct comparisons with conventional catalysts are often lacking, making it difficult to assess their relative efficiency and practical advantages. Challenges related to catalyst deactivation, structural degradation, and scalability must be addressed to enable their effective implementation in real energy systems.

3.12. Solar Energy Conversion

Nanostructured materials have significantly improved the performance of solar energy conversion systems, including photovoltaic devices and photocatalytic systems [16,17]. Green-synthesized nanomaterials can be used as light absorbers, charge transport materials, or catalytic components in solar-driven processes [16,20]. In photovoltaic applications, nanostructures such as quantum dots, metal oxides, and hybrid nanocomposites enhance light absorption and charge separation, leading to improved energy conversion efficiency [16]. The use of green synthesis routes reduces the environmental footprint of these materials and supports the development of sustainable solar technologies [26]. Photocatalytic systems for solar fuel generation, such as hydrogen production and carbon dioxide reduction, also benefit from green-synthesized nanomaterials [3,16]. These systems utilize solar energy to drive chemical reactions, offering a renewable pathway for fuel production [15]. Although green-synthesized nanomaterials have shown promising performance in solar energy conversion, their efficiency and long-term stability often remain lower than those of conventional materials optimized through well-established fabrication methods. In addition, challenges related to charge recombination, material degradation under prolonged irradiation, and limited scalability continue to hinder practical applica-

tions. These limitations highlight the need for improved material design and more rigorous performance evaluation under real operating conditions.

3.13. Energy Storage Systems

Energy storage technologies, including batteries and supercapacitors, are essential for the efficient utilization of renewable energy sources [15,16]. Nanostructured materials have been extensively explored for these applications due to their high surface area, short diffusion paths, and enhanced electrochemical properties [15]. Green-synthesized nanomaterials, particularly carbon-based materials, metal oxides, and hybrid nanocomposites, have demonstrated excellent performance in energy storage devices [8,20]. In lithium-ion batteries, nanostructured electrodes improve charge capacity, cycling stability, and rate performance [15]. In supercapacitors, these materials contribute to high power density and rapid charge-discharge cycles [15]. The incorporation of biocompatible and sustainably produced nanomaterials into energy storage systems not only enhances performance but also reduces environmental impact, aligning with the principles of green energy technologies [26]. Despite the promising electrochemical performance of green-synthesized nanomaterials, their practical application in energy storage systems is still limited by challenges related to long-term cycling stability, electrode degradation, and scalability of synthesis methods. Furthermore, inconsistencies in material properties arising from biological synthesis routes can affect reproducibility and device performance. Addressing these limitations will be essential for the integration of these materials into reliable and commercially viable energy storage technologies.These limitations are consistent with broader challenges in the field, including large-scale production, long-term stability, and cost-effectiveness of green-synthesized nanomaterials for energy applications [15]. Further research is needed to optimize synthesis methods, improve material performance, and integrate these nanostructures into practical energy systems.

4. Challenges and Future Perspectives

Despite the significant progress achieved in the development of green-synthesized metal-based and hybrid nanomaterials, several critical challenges remain that limit their translation from laboratory research to real-world applications. Addressing these limitations requires a deeper understanding of synthesis mechanisms, improved standardization, and the integration of multidisciplinary approaches. The main challenges, proposed strategies, and future perspectives for green-synthesized nanostructures are summarized in Figure 3. A comparison between green and conventional synthesis methods for nanomaterials is presented in Table 2.

Table 2. Comparison between green and conventional synthesis methods for nanomaterials.

Parameter	Green Synthesis	Conventional Methods
Toxicity	Low; uses biological or benign agents	High; often involves toxic chemicals
Environmental impact	Environmentally friendly; minimal hazardous waste	Generates hazardous byproducts and waste
Energy consumption	Low to moderate; mild reaction conditions	High; often requires elevated temperature and pressure
Scalability	Limited; still under development	Well-established industrial processes
Reproducibility	Variable; influenced by biological variability	High; controlled and standardized processes
Cost	Potentially low; uses renewable resources	High; dependent on chemicals and energy input
Yield	Moderate; depends on biological system	High; optimized for industrial production

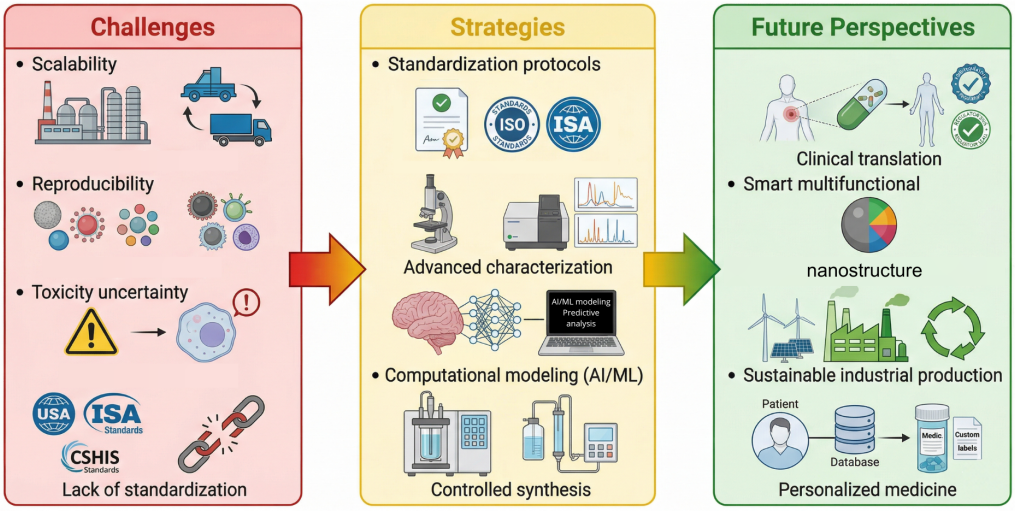


Figure 3. Key Challenges, Strategies, and Future Perspectives regarding Green-Synthesized. Arrows indicate the conceptual progression from challenges to strategies and future perspectives. Colors are used to distinguish thematic panels and schematic elements. The red exclamation mark denotes toxicity/safety uncertainty. The colored lines above the computer graphic represent illustrative characterization/modeling outputs, and the pie chart colors schematically indicate multifunctionality rather than quantitative proportions. Source: Created by the authors.

4.1. Lack of Mechanistic Understanding

One of the major scientific gaps in green nanotechnology lies in the limited mechanistic understanding of biological synthesis processes [14,20]. Although plant extracts, microorganisms, and biomolecules are widely used as reducing and stabilizing agents, the exact pathways governing nucleation, growth, and stabilization of nanostructures remain poorly defined [6,19].

The complexity and variability of biological systems introduce significant uncertainty in controlling nanoparticle properties, such as size distribution, morphology, and surface chemistry [20]. This lack of predictability hampers reproducibility and limits the rational design of nanomaterials for specific applications [8]. Future research should focus on elucidating these mechanisms through advanced analytical techniques and computational modeling, enabling a more controlled and predictable synthesis process [14].

4.2. Reproducibility and Standardization Issues

Reproducibility remains a major bottleneck in the field of green synthesis [2,6]. Variations in biological sources—such as seasonal differences in the phytochemical profiles of plant hydrolates and essential oils—extraction methods, and experimental conditions can lead to significant inconsistencies in nanoparticle characteristics [14]. This issue is particularly critical for biomedical applications, where precise control over material properties is essential [8].

Currently, there is a lack of standardized protocols for green synthesis, characterization, and performance evaluation [3]. The absence of universally accepted guidelines makes it difficult to compare results across studies and slows down technological advancement [20]. Establishing standardized methodologies and reporting frameworks will be essential to ensure reproducibility and facilitate regulatory approval [2].

4.3. Scalability and Industrial Translation

While green synthesis methods are often described as cost-effective and environmentally friendly, their scalability remains a significant challenge [2,20]. Biological processes may require longer reaction times, controlled conditions, and complex downstream processing, which can limit their feasibility for large-scale production [6,14].

Moreover, the transition from laboratory-scale synthesis to industrial manufacturing requires consistent quality, high yield, and economic viability [3]. The development of scalable green synthesis platforms, such as continuous-flow systems, bioreactor-based approaches, and the utilization of agro-industrial residues to lower production costs, represents a promising direction for overcoming these limitations [2,8].

4.4. Toxicological and Environmental Uncertainties

Although green-synthesized nanomaterials are generally considered more biocompatible, comprehensive evaluation of their long-term toxicity and environmental impact is still lacking [2,6]. The interaction of nanomaterials with biological systems is highly complex and depends on multiple factors, including size, shape, surface chemistry, and dosage [10].

In addition, the fate and transformation of nanomaterials in environmental systems remain poorly understood [4]. Potential risks associated with bioaccumulation, persistence, and unintended ecological effects must be carefully assessed [4,11]. Future studies should adopt standardized toxicological frameworks and life cycle assessment approaches to ensure the safe implementation of nanotechnology [3].

4.5. Regulatory and Translational Barriers

The translation of nanomaterials into clinical and industrial applications is further hindered by regulatory challenges [3,10]. The lack of clear regulatory guidelines specific to green-synthesized nanomaterials complicates their approval process, particularly in the biomedical field [8].

Bridging the gap between academic research and industrial application will require closer collaboration between scientists, engineers, regulatory agencies, and industry stakeholders [4]. Developing clear regulatory pathways and validation protocols will be essential for accelerating commercialization [11].

4.6. Future Perspectives

To address these challenges, future research should prioritize the development of standardized synthesis protocols, enabling reproducibility across different biological systems and experimental conditions. The integration of advanced characterization techniques with machine learning and computational modeling can provide predictive control over nanoparticle formation and properties. Scalable production strategies, such as continuous-flow synthesis and bioreactor-based approaches, should be further explored to facilitate industrial translation. Furthermore, comprehensive toxicological assessments and life cycle analyses are essential to ensure the safe and sustainable implementation of green-synthesized nanomaterials. Collaborative efforts between academia, industry, and regulatory agencies will be critical to establish clear guidelines and accelerate the practical application of these technologies. In this context, the development of smart and multifunctional metal-based and hybrid nanomaterials, capable of performing multiple tasks simultaneously, represents a key direction for next-generation applications [6].

In nanomedicine, efforts should be directed toward improving targeting efficiency, minimizing off-target effects, and enhancing clinical translation through robust preclinical validation [3,4]. In environmental and energy applications, the design of recyclable, stable, and high-performance nanomaterials will be critical for sustainable implementation [9,16].

Furthermore, the convergence of green chemistry, materials science, and biotechnology is expected to drive the development of innovative synthesis strategies and multifunctional systems [19]. By addressing current challenges and leveraging interdisciplinary approaches, green-synthesized biocompatible nanostructures have the potential to play a transformative role in advancing sustainable technologies and improving global health [8,20].

To further advance the field toward practical implementation, future research should adopt more actionable and standardized frameworks. In particular, the establishment of standardized characterization and reporting checklists is essential to ensure consistency across studies, including parameters such as nanoparticle size distribution, surface chemistry, zeta potential, and biological response metrics [1]. In addition, batch-to-batch reproducibility should be quantitatively assessed using defined statistical metrics to evaluate synthesis reliability [7]. The development of minimum toxicological evaluation panels, including cytotoxicity, hemocompatibility, oxidative stress, and long-term exposure studies, is critical for biomedical applications [10]. From a technological perspective, scalable production strategies such as continuous-flow synthesis and bioreactor-based systems should be further explored to bridge the gap between laboratory-scale and industrial manufacturing [12,22]. Furthermore, the integration of life-cycle assessment (LCA) approaches is necessary to evaluate the environmental impact of green-synthesized nanomaterials throughout their production, use, and disposal [15]. These measures will be essential to support regulatory approval and enable the safe and sustainable deployment of green nanotechnology.

5. Conclusions

Green synthesis has become an important strategy for the fabrication of functional nanomaterials, offering alternative routes to conventional physicochemical methods [2,20]. By leveraging biological systems such as plant extracts, microorganisms, and biomolecules, this approach enables the production of nanomaterials with intrinsic surface functionalization and controlled physicochemical properties, which are advantageous for biomedical and environmental applications [8,14].

The versatility of green-synthesized nanostructures has been demonstrated across a wide range of domains, including nanomedicine, environmental remediation, and energy systems [3,26]. However, future progress in these areas will depend on the development of more systematic and quantitative evaluation frameworks that allow direct comparison between materials, synthesis routes, and application performance.

Despite these promising developments, several challenges remain, including limited mechanistic understanding, reproducibility issues, scalability constraints, and concerns related to long-term toxicity and regulatory approval. Addressing these limitations will require interdisciplinary efforts combining advanced characterization techniques, computational modeling, and standardized methodologies to enable precise control over nanomaterial synthesis and performance [3,6].

To further overcome these limitations, future research should prioritize the establishment of standardized synthesis and characterization protocols, enabling reproducibility across different biological systems and experimental conditions. In addition, the integration of advanced characterization techniques with machine learning and computational modeling is expected to provide predictive control over nanomaterial synthesis and properties.

Particular attention should also be given to application-oriented validation, including in vivo studies in nanomedicine, realistic environmental conditions for remediation systems, and long-term stability assessments in energy technologies. These efforts will be essential to bridge the gap between laboratory-scale demonstrations and real-world implementation. Furthermore, scalable production strategies, such as continuous-flow syn-

thesis and bioreactor-based approaches, must be further developed to support industrial translation. The establishment of clear regulatory frameworks and standardized evaluation methodologies will also be critical to ensure the safe and effective deployment of green-synthesized nanomaterials.

Overall, this mini-review highlights that the integration of green chemistry principles with emerging technologies such as machine learning, synthetic biology, and nanomanufacturing can accelerate the development of next-generation nanomaterials. However, future progress will depend on moving beyond qualitative descriptions toward quantitative, standardized, and application-driven evaluation of green-synthesized nanomaterials. By addressing current challenges and fostering collaboration between academia, industry, and regulatory bodies, these systems have strong potential to contribute to sustainable technologies and improved global health outcomes.

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